



Clinical trial results:

A Phase 4 Open Label, Prospective Study in Patients With Pompe Disease to Evaluate the Efficacy and Safety of Alglucosidase Alfa Produced at the 4000 L Scale

Summary

EudraCT number	2015-000512-18
Trial protocol	Outside EU/EEA
Global end of trial date	29 December 2014

Results information

Result version number	v2 (current)
This version publication date	17 July 2016
First version publication date	25 June 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data setClarification of unit of measure in endpoint analysis.

Trial information

Trial identification

Sponsor protocol code	AGLU09411/EFC12720
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01526785
WHO universal trial number (UTN)	U1111-1162-8919

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	500 Kendall Street, Cambridge, MA, United States, 02142
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary efficacy objective was to demonstrate comparability of treatment with alglucosidase alfa produced at the 4000L scale in subjects previously treated with 160L scale alglucosidase alfa.

Protection of trial subjects:

Pediatric Subjects: The study was conducted by investigators experienced in the treatment of pediatric subjects. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Adult Subjects: Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.

Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 March 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 113
Worldwide total number of subjects	113
EEA total number of subjects	0

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	33
Children (2-11 years)	73
Adolescents (12-17 years)	6
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted in United States. A total of 113 subjects were treated between 9 March 2012 and 4 June 2014.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Alglucosidase Alfa
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Arm description:

Alglucosidase alfa produced at 4000 L scale for 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Alglucosidase Alfa
Investigational medicinal product code	
Other name	Lumizyme®
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

4000 L alglucosidase alfa as per subject's routine practice.

Number of subjects in period 1	Alglucosidase Alfa
Started	113
Completed	100
Not completed	13
Consent withdrawn by subject	2
Physician decision	1
Death	2
Study Terminated by Sponsor	8

Baseline characteristics

Reporting groups

Reporting group title	Alglucosidase Alfa
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Reporting group description:

Alglucosidase alfa produced at 4000 L scale for 52 weeks.

Reporting group values	Alglucosidase Alfa	Total	
Number of subjects	113	113	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	4.8		
standard deviation	± 3.73	-	
Gender categorical			
Units: Subjects			
Female	53	53	
Male	60	60	

End points

End points reporting groups

Reporting group title	Alglucosidase Alfa
Reporting group description: Alglucosidase alfa produced at 4000 L scale for 52 weeks.	

Primary: Percentage of Subjects Who were Clinically Stable or Improved at Week 52

End point title	Percentage of Subjects Who were Clinically Stable or Improved at Week 52 ^[1]
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End point description:

Clinical stability defined as absence of death due to disease progression or new dependency on invasive ventilation and; decline in cardiac status, motor function, and pulmonary function from baseline. Analysis was carried out on full analysis population defined as all subjects who receive at least 1 infusion of 4000 L alglucosidase alfa during the study.

End point type	Primary
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End point timeframe:

Week 52

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses for this endpoint

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	104			
Units: percentage of subjects				
number (confidence interval 95%)	83.7 (75.1 to 90.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Survival Rate at Week 52

End point title	Survival Rate at Week 52
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End point description:

Percentage of subjects who were alive at Week 52, were reported. Survival rate was calculated by Kaplan-Meier estimate. Analysis was carried out on full analysis population.

End point type	Secondary
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End point timeframe:

Week 52

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	113			
Units: percentage of subjects				
number (confidence interval 95%)	98.1 (92.73 to 99.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Invasive Ventilator-Free Survival Rate at Week 52

End point title	Invasive Ventilator-Free Survival Rate at Week 52
End point description: Percentage of subjects who were invasive ventilator-free at week 52, were reported. Invasive ventilation was defined as mechanical ventilatory support applied with the use of an endotracheal tube or tracheostomy. Invasive ventilator-free survival rate was calculated by Kaplan-Meier estimate. Analysis was carried out on full analysis population.	
End point type	Secondary
End point timeframe: Week 52	

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: percentage of subjects				
number (confidence interval 95%)	92.4 (83.89 to 96.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on Left Ventricular Mass Z-Score (LVM-Z) at Week 52

End point title	Change From Baseline on Left Ventricular Mass Z-Score (LVM-Z) at Week 52
End point description: Z--Scores indicate the number of standard deviations (SD) from the mean in a normal distribution. A negative change from baseline indicates a decrease and positive change from baseline indicates an increase in LVM-Z score. The normal range is -2 to 2 and greater than 2 may indicate left ventricular hypertrophy. Analysis was carried out on full analysis population.	
End point type	Secondary
End point timeframe: Baseline, Week 52	

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	67			
Units: Z score				
arithmetic mean (standard deviation)	-0.5 (\pm 1.71)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on Gross Motor Function Measure-88 (GMFM-88) at Week 52

End point title	Change From Baseline on Gross Motor Function Measure-88 (GMFM-88) at Week 52
End point description:	
GMFM-88 (88-item measure to detect gross motor function) consists of 5 components, each measured on a 4-point Likert scale. The score for each dimension was expressed as a percentage of the maximum score for that dimension. Total score ranges from 0% to 100%, where higher scores indicate better motor functions. Analysis was carried out on full analysis population. Number of subjects analysed = subjects with baseline and Week 52 GMFM-88 data.	
End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	90			
Units: percentage of total score				
arithmetic mean (standard deviation)	3.7 (\pm 17.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Vital Capacity (FVC) at Week 52- At Supine Position

End point title	Change From Baseline in Forced Vital Capacity (FVC) at Week 52- At Supine Position
End point description:	
Percent predicted FVC values are reported. FVC is the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Predicted forced vital capacity is based on a	

formula using sex, age, and height of a person, and is an estimate of healthy lung capacity. Percent of predicted FVC = (observed value)/(predicted value) * 100%. Analysis was carried out on full analysis population. Number of subjects analysed = subjects with baseline and Week 52 FVC data.

End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: percent predicted FVC				
arithmetic mean (standard deviation)	3.2 (± 11.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Vital Capacity (FVC) at Week 52- At Sitting Position

End point title	Change From Baseline in Forced Vital Capacity (FVC) at Week 52- At Sitting Position
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End point description:

Percent predicted FVC values are reported. FVC is the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Predicted forced vital capacity is based on a formula using sex, age, and height of a person, and is an estimate of healthy lung capacity. Percent of predicted FVC = (observed value)/(predicted value) * 100%. Analysis was carried out on full analysis population. Number of subjects analysed = subjects with baseline and Week 52 FVC data.

End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percent predicted FVC				
arithmetic mean (standard deviation)	2.3 (± 11.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (Week 52) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported adverse events are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (from the first infusion of study drug up to 30 days after last infusion of study drug). Analysis was performed on safety population which included all treated subjects.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Alglucosidase Alfa 4000 L
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Reporting group description:

Alglucosidase alfa produced at 4000 L scale for 52 weeks.

Serious adverse events	Alglucosidase Alfa 4000 L		
Total subjects affected by serious adverse events			
subjects affected / exposed	73 / 113 (64.60%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events			
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jugular Vein Thrombosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Central Venous Catheterisation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Therapeutic Procedure			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Chills			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Device Malfunction			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device Breakage			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypothermia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oedema Peripheral			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	10 / 113 (8.85%)		
occurrences causally related to treatment / all	4 / 16		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Acute Respiratory Distress Syndrome				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Acute Respiratory Failure				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Apnoea				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aspiration				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atelectasis				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Bronchial Secretion Retention				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchiectasis				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Chronic Respiratory Failure				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				

subjects affected / exposed	5 / 113 (4.42%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Cough			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumonia Aspiration			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary Granuloma			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory Disorder			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory Distress			
subjects affected / exposed	16 / 113 (14.16%)		
occurrences causally related to treatment / all	0 / 23		
deaths causally related to treatment / all	0 / 2		
Respiratory Failure			

subjects affected / exposed	7 / 113 (6.19%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 1		
Rhonchi			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory Tract Congestion			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Mental Status Changes			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Self-Injurious Ideation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood Albumin Decreased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Oxygen Saturation Decreased subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Gamma-Glutamyltransferase Increased				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Feeding Tube Complication				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Foreign Body				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femur Fracture				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Foreign Body Aspiration				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Traumatic Haemothorax				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tracheal Obstruction				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Cardiac disorders			
Bradycardia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac Arrest			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac Failure Congestive			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-Respiratory Arrest			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Cardiopulmonary Failure			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cyanosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Left Ventricular Hypertrophy			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Mitral Valve Incompetence			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulseless Electrical Activity			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Sinus Tachycardia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Supraventricular Tachycardia			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Brain Injury			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral Ischaemia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Convulsion			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gross Motor Delay			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Loss Of Consciousness			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tremor			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Motion Sickness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Eyelid Ptosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal Pain			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Dental Caries			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Diarrhoea			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal Disorder			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intussusception			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis Acute			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			

Purpura			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperhidrosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary Retention			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscular Weakness			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Muscle Contracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Adenovirus Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			

subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bacterial Tracheitis				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchiolitis				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Device Related Infection				
subjects affected / exposed	6 / 113 (5.31%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis Viral				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haemophilus Bacteraemia				

subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Klebsiella Bacteraemia				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lobar Pneumonia				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lung Infection				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metapneumovirus Infection				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Otitis Media Acute				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Parainfluenzae Virus Infection				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Periumbilical Abscess				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	25 / 113 (22.12%)			
occurrences causally related to treatment / all	0 / 33			
deaths causally related to treatment / all	0 / 1			
Pneumonia Parainfluenzae Viral				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia Respiratory Syncytial Viral				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonia Pseudomonal				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia Viral				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Respiratory Syncytial Virus Bronchiolitis				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory Syncytial Virus Infection				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory Tract Infection				
subjects affected / exposed	4 / 113 (3.54%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Rhinovirus Infection				

subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Respiratory Tract Infection Viral				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Staphylococcal Infection				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tracheitis				
subjects affected / exposed	5 / 113 (4.42%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Tracheostomy Infection				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary Tract Infection				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Upper Respiratory Tract Infection				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Urinary Tract Infection Bacterial				

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection Staphylococcal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral Infection			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Failure To Thrive			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fluid Overload			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Alglucosidase Alfa 4000 L		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	113 / 113 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cholesteatoma			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Vascular disorders			
Aortic Dilatation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Flushing			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	13		
Hypertension			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Haematoma			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Pallor			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Peripheral Coldness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Surgical and medical procedures			
Central Venous Catheterisation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		

Ear Tube Removal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gastrostomy Tube Removal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
General disorders and administration site conditions			
Abasia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Catheter Site Erythema			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Catheter Site Haemorrhage			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Catheter Site Extravasation			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
Catheter Site Inflammation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Catheter Site Oedema			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Catheter Site Pain			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Catheter Site Rash			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Catheter Site Related Reaction			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Catheter Site Swelling			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Chest Discomfort			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Chills			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Chest Pain			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	8		
Crepitations			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Device Breakage			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Device Dislocation			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	6		
Device Issue			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Device Malfunction			
subjects affected / exposed	9 / 113 (7.96%)		
occurrences (all)	21		
Device Occlusion			
subjects affected / exposed	13 / 113 (11.50%)		
occurrences (all)	15		
Discomfort			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Disease Progression			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Energy Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Extravasation			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Feeling Hot			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gait Disturbance			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Granuloma			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	5		
Gravitational Oedema			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Influenza Like Illness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Infusion Site Extravasation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Infusion Site Swelling			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Injection Site Extravasation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Injection Site Swelling			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Oedema			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Malaise			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Oedema Peripheral			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Peripheral Swelling			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
Pyrexia			
subjects affected / exposed	61 / 113 (53.98%)		
occurrences (all)	218		
Secretion Discharge			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	9		
Thirst			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Thrombosis In Device			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Immune system disorders			
Food Allergy			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Drug Hypersensitivity			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		

Hypersensitivity subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 5		
Multiple Allergies subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Seasonal Allergy subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Reproductive system and breast disorders			
Genital Discomfort subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Vaginal Prolapse subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Vulvovaginal Disorder subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Vulvovaginal Erythema subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Vulvovaginal Pruritus subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Respiratory, thoracic and mediastinal disorders			
Adenoidal Hypertrophy subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Aspiration subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 3		
Atelectasis subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 6		
Bronchial Hyperreactivity			

subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
Bronchial Secretion Retention			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	6		
Bronchial Wall Thickening			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Bronchomalacia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Bronchospasm			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Choking			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	5		
Cough			
subjects affected / exposed	36 / 113 (31.86%)		
occurrences (all)	105		
Dysphonia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	11		
Epistaxis			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Haemoptysis			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	5		
Hypercapnia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hypoventilation			

subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Hypoxia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Increased Bronchial Secretion			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Increased Upper Airway Secretion			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	11		
Increased Viscosity Of Bronchial Secretion			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Nasal Congestion			
subjects affected / exposed	16 / 113 (14.16%)		
occurrences (all)	23		
Nasal Discharge Discolouration			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Nasal Dryness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Oropharyngeal Pain			
subjects affected / exposed	13 / 113 (11.50%)		
occurrences (all)	14		
Pleural Effusion			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Pneumonia Aspiration			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
Productive Cough			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		

Pulmonary Artery Dilatation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Pulmonary Congestion			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Respiratory Disorder			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Pulmonary Hypertension			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Respiratory Distress			
subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	10		
Respiratory Failure			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Respiratory Muscle Weakness			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Respiratory Tract Congestion			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	8		
Respiratory Tract Haemorrhage			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	4		
Rhinitis Allergic			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Rhinorrhoea			
subjects affected / exposed	24 / 113 (21.24%)		
occurrences (all)	42		
Rhonchi			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		

Sleep Apnoea Syndrome			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Sinus Congestion			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Sneezing			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Snoring			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Sputum Discoloured			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Sputum Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Tachypnoea			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Throat Irritation			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Throat Tightness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	3		
Tonsillar Hypertrophy			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Tracheal Ulcer			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Upper Respiratory Tract Congestion			
subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	14		

Upper-Airway Cough Syndrome subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 2		
Use Of Accessory Respiratory Muscles subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 2		
Wheezing subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 6		
Psychiatric disorders			
Aggression subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 2		
Agitation subjects affected / exposed occurrences (all)	4 / 113 (3.54%) 7		
Anxiety subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 5		
Bruxism subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Attention Deficit/Hyperactivity Disorder subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Insomnia subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 5		
Irritability subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Mental Disorder subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Mood Swings			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Oppositional Defiant Disorder			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Sleep Disorder			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Investigations			
Alanine Aminotransferase Abnormal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Alanine Aminotransferase Increased			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
Aspartate Aminotransferase Abnormal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Aspartate Aminotransferase Increased			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
Atrial Pressure Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Creatine Phosphokinase Abnormal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Creatine Phosphokinase Mb Increased			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	7		
Blood Culture Positive			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	7		
Blood Lactate Dehydrogenase Abnormal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Blood Potassium Decreased			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Blood Pressure Decreased			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Blood Pressure Increased			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	8		
Blood Pressure Systolic Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Uric Acid Decreased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Uric Acid Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Zinc Decreased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Body Temperature Increased			

subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Brain Natriuretic Peptide Increased			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Breath Sounds Abnormal			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Creatine Urine Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Creatinine Urine Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Electrocardiogram Pr Shortened			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Electrocardiogram St Segment Elevation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Electrocardiogram Qt Prolonged			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eosinophil Count Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Electrocardiogram Abnormal			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Haematocrit Decreased			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Haemoglobin Decreased			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
Heart Rate Increased			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Liver Function Test Abnormal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Neutrophil Count Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Neutrophil Count Abnormal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Occult Blood Positive			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Neutrophil Percentage Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Oxygen Saturation Decreased			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	6		
Platelet Count Increased			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Protein Urine			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Protein Urine Present			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Pulmonary Function Test Decreased			

subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Pulse Pressure Abnormal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Respiratory Rate Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Specific Gravity Urine			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Serum Ferritin Decreased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Sputum Culture Positive			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Staphylococcus Test Positive			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Urine Ketone Body Present			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tuberculin Test Positive			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Urine Output Decreased			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Weight Decreased			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Weight Increased			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
White Blood Cell Count Abnormal			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
White Blood Cell Count Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Agitation Postoperative			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Animal Bite			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Ankle Fracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Animal Scratch			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Arthropod Bite			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	8		
Arthropod Sting			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Concussion			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	7		
Exposure To Communicable Disease			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eye Contusion			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eye Injury			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Face Injury			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	11 / 113 (9.73%)		
occurrences (all)	13		
Feeding Tube Complication			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Femur Fracture			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Gastrointestinal Anastomotic Leak			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	3		
Foreign Body			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gastrointestinal Stoma Complication			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hand Fracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Head Injury			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Joint Dislocation			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Humerus Fracture			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Laryngeal Injury			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Laceration			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	6		
Ligament Sprain			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Limb Injury			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Lower Limb Fracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Overdose			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Periorbital Haemorrhage			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Post Procedural Haemorrhage			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Postoperative Respiratory Distress			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Postoperative Fever			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Procedural Nausea			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Procedural Pain			

subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	10		
Procedural Vomiting			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Scratch			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Skin Wound			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Skin Abrasion			
subjects affected / exposed	9 / 113 (7.96%)		
occurrences (all)	14		
Soft Tissue Injury			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Splinter			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Stoma Site Erythema			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Stoma Site Irritation			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Stoma Site Haemorrhage			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Stoma Site Reaction			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Stoma Site Rash			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Thermal Burn			

subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Sunburn			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tooth Avulsion			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tibia Fracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tooth Fracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tooth Injury			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tracheostomy Malfunction			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Vaccination Complication			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Wound			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Wound Dehiscence			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Cardiac disorders			

Arrhythmia			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Bundle Branch Block Right			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Bradycardia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	4		
Cardiac Failure			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Cardiomyopathy			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Diastolic Dysfunction			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Defect Conduction Intraventricular			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Heart Valve Incompetence			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Left Ventricular Dysfunction			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Pericardial Effusion			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	6		
Right Atrial Dilatation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Right Ventricular Hypertrophy			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		

Sinus Tachycardia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Sinus Bradycardia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Tachycardia			
subjects affected / exposed	13 / 113 (11.50%)		
occurrences (all)	21		
Supraventricular Tachycardia			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	13		
Wolff-Parkinson-White Syndrome			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Tricuspid Valve Incompetence			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Nervous system disorders			
Allodynia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Areflexia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Burning Sensation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Clumsiness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Convulsion			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Dizziness			

subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Facial Paresis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Formication			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gross Motor Delay			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	14 / 113 (12.39%)		
occurrences (all)	36		
Hypoaesthesia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Hyporeflexia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Hypotonia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Lethargy			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	8		
Motor Developmental Delay			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Motor Dysfunction			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Muscle Contractions Involuntary			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Nystagmus			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Paralysis Flaccid			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Poor Quality Sleep			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Psychomotor Hyperactivity			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Somnolence			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Speech Disorder			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	8		
Coagulopathy			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eosinophilia			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	7		

Iron Deficiency Anaemia subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Lymphadenitis subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Neutropenia subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Ear and labyrinth disorders			
Cerumen Impaction subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 5		
Conductive Deafness subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Deafness subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Deafness Neurosensory subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Deafness Unilateral subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Ear Pain subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 8		
Eustachian Tube Dysfunction subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 5		
Middle Ear Effusion			

subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Otorrhoea			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Mixed Deafness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tympanic Membrane Disorder			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tympanic Membrane Perforation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eye disorders			
Blepharitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Astigmatism			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Chalazion			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Conjunctival Hyperaemia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eye Discharge			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Dry Eye			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
Eye Pruritus			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		

Eye Irritation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eye Swelling			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eyelid Ptosis			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	6		
Eyelid Oedema			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hypermetropia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Lid Sulcus Deepened			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Ocular Hyperaemia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Myopia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Photophobia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Strabismus			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Vision Blurred			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal Discomfort			

subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Abdominal Distension			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Abdominal Pain			
subjects affected / exposed	10 / 113 (8.85%)		
occurrences (all)	17		
Abnormal Faeces			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Abdominal Pain Upper			
subjects affected / exposed	11 / 113 (9.73%)		
occurrences (all)	18		
Anal Fissure			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Aphthous Stomatitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	20 / 113 (17.70%)		
occurrences (all)	23		
Dental Caries			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Dental Discomfort			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Dysphagia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	55 / 113 (48.67%)		
occurrences (all)	121		
Faecal Incontinence			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Faeces Discoloured			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Flatulence			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Gastric Ulcer			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Frequent Bowel Movements			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	3		
Gastrointestinal Disorder			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	10		
Gastritis			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Gastrooesophageal Reflux Disease			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Gingival Bleeding			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Haematochezia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Haemorrhoids			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Ileus			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Lip Blister			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Infrequent Bowel Movements			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Mouth Ulceration			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Lip Ulceration			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	12 / 113 (10.62%)		
occurrences (all)	20		
Oral Disorder			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Rectal Fissure			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Regurgitation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Retained Deciduous Tooth			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Retching			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Salivary Hypersecretion			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Sensitivity Of Teeth			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Teething			

subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Tongue Spasm			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tooth Deposit			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Tooth Impacted			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	42 / 113 (37.17%)		
occurrences (all)	112		
Hepatobiliary disorders			
Hepatic Fibrosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Cholelithiasis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Alopecia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Blister			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Cold Sweat			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Decubitus Ulcer			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Dermatitis			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Dermatitis Allergic			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Dermatitis Diaper			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	6		
Dermatitis Contact			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Dry Skin			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Ecchymosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	9		
Excessive Granulation Tissue			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
Granuloma Skin			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hyperhidrosis			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Hyperkeratosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Ingrowing Nail			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Ingrown Hair			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Macule			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Mechanical Urticaria			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Papule			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	3		
Petechiae			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Photosensitivity Reaction			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	6		
Pruritus Generalised			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	31 / 113 (27.43%)		
occurrences (all)	42		
Rash Erythematous			

subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Rash Macular			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Rash Pruritic			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Red Man Syndrome			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Skin Disorder			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Seborrhoeic Dermatitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Skin Exfoliation			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Skin Hyperpigmentation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Skin Irritation			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Skin Lesion			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Skin Ulcer			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Swelling Face			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Urticaria			

subjects affected / exposed	9 / 113 (7.96%)		
occurrences (all)	28		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Haematuria			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Incontinence			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Nephrolithiasis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Pollakiuria			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Proteinuria			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Urinary Hesitation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Urinary Incontinence			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Urinary Retention			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Endocrine disorders			
Precocious Puberty			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	7		
Arthropathy			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Back Pain			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	6		
Axillary Mass			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Foot Deformity			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Deformity Thorax			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Fracture Pain			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hip Deformity			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Joint Contracture			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Joint Stiffness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Joint Swelling			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Kyphosis			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		

Limb Discomfort			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Muscle Contracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Muscle Spasms			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Muscle Tightness			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Muscular Weakness			
subjects affected / exposed	12 / 113 (10.62%)		
occurrences (all)	15		
Musculoskeletal Pain			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
Musculoskeletal Chest Pain			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Musculoskeletal Stiffness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Myopathy			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Neck Pain			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	5		
Osteopenia			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		

Pain In Jaw			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	3		
Pain In Extremity			
subjects affected / exposed	16 / 113 (14.16%)		
occurrences (all)	23		
Scoliosis			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	6		
Tendinous Contracture			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Tendon Discomfort			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Tendon Disorder			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Infections and infestations			
Abscess Limb			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Acarodermatitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Adenovirus Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Atypical Pneumonia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Bacterial Tracheitis			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	7		
Beta Haemolytic Streptococcal Infection			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Body Tinea			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Bronchiolitis			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Candida Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	8		
Chronic Sinusitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Cellulitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Clostridium Difficile Colitis			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Conjunctivitis			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	9		
Croup Infectious			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Ear Infection			
subjects affected / exposed	12 / 113 (10.62%)		
occurrences (all)	20		
Device Related Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Enterovirus Infection			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Ear Lobe Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Escherichia Urinary Tract Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Erythema Infectiosum			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Folliculitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eye Infection			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Fungal Infection			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Fungal Skin Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Furuncle			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	11 / 113 (9.73%)		
occurrences (all)	15		
Gastroenteritis Viral			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Gastroenteritis Norovirus			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gastrointestinal Infection			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Gingival Abscess			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gingivitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Haemophilus Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hand-Foot-And-Mouth Disease			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Herpes Zoster			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hordeolum			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	5		
Impetigo			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	10		
Labyrinthitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Lice Infestation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Lobar Pneumonia			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Lip Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Nail Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	12 / 113 (10.62%)		
occurrences (all)	23		
Oral Candidiasis			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
Oral Herpes			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Otitis Externa Fungal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Otitis Externa			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	5		
Otitis Media			
subjects affected / exposed	23 / 113 (20.35%)		
occurrences (all)	35		
Otitis Media Acute			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	7		
Otitis Media Chronic			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	6		
Pharyngitis			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	14		
Pharyngitis Streptococcal			

subjects affected / exposed	13 / 113 (11.50%)		
occurrences (all)	24		
Pneumonia			
subjects affected / exposed	17 / 113 (15.04%)		
occurrences (all)	32		
Pneumonia Viral			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Pseudomonas Infection			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
Rash Pustular			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Respiratory Tract Infection			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Respiratory Syncytial Virus Infection			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Rhinitis			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	8		
Rhinovirus Infection			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
Rotavirus Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	6		
Skin Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Staphylococcal Infection			

subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	5		
Stoma Site Infection			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Streptococcal Infection			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Streptococcal Urinary Tract Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Subcutaneous Abscess			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Tinea Infection			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Tooth Abscess			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Tonsillitis			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Tracheitis			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	12		
Tooth Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tracheobronchitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tracheostomy Infection			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	9		
Upper Respiratory Tract Infection			

Bacterial			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Upper Respiratory Tract Infection			
subjects affected / exposed	49 / 113 (43.36%)		
occurrences (all)	104		
Urinary Tract Infection			
subjects affected / exposed	19 / 113 (16.81%)		
occurrences (all)	31		
Viral Infection			
subjects affected / exposed	15 / 113 (13.27%)		
occurrences (all)	23		
Viral Rash			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	7		
Vulvovaginal Mycotic Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Abnormal Weight Gain			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Decreased Appetite			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Dehydration			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	7		
Electrolyte Imbalance			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Failure To Thrive			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hypochloraemia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hypoalbuminaemia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Iron Deficiency			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Vitamin D Deficiency			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 October 2012	6-month administrative analysis was added. -For the primary efficacy endpoint, in addition to the analysis using the full analysis set specified in the original protocol, the analysis was also to be conducted on the Per-Protocol Analysis Set. -The efficacy endpoint of left ventricular mass index Z- score (LVMI-Z) was revised to LVM-Z. -Shortening of the post-infusion observation period was changed from being allowed after a 6-month treatment period to being allowed after a 3-month treatment period. -Home infusions were changed from being allowed after 4 infusions in subjects with no history of moderate or severe infusion-associated reactions (IARs) or serious adverse events (SAEs) to being allowed after 2 infusions in subjects with no history of moderate or severe IARs or SAEs. -The Sponsor's department name, Global Patient Safety and Risk Management, was updated for a recent name change to Global Pharmacovigilance and Epidemiology. -Text was added to clarify that pulmonary function tests were not required in young subjects unable to undergo testing. -The protocol was modified to ensure that subject position during measurement of vital signs was to be recorded in the electronic case report form and that vital signs and weight were to be obtained at every study visit. -The IgG antibodies, inhibitory antibodies, and urine pregnancy testing schedules were clarified. -Text referring to subjects' previous treatment "in the commercial setting" was deleted as subjects treated with 160L scale product in other clinical trials were eligible to enroll. - Measurement of R voltage V6 and S voltage V1 were removed from the ECG. -Text was deleted to reflect that efficacy and safety results would not be summarized by baseline Pompe disease status. - The presentation of results of planned clinical laboratory assessments was clarified. -The stipulation that the Data Safety Monitoring Board (DSMB) would be comprised of 4 physicians was removed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported